REMARKS

Applicants submit this response to the Office Action dated June 1, 2006. Claims 97-100 were withdrawn from consideration as being drawn to a non-elected invention. Claims 88-96 are pending.

Applicants acknowledge that the Declaration under 37 C.F.R. § 1.132 filed March 8, 2006 has been entered in full and that the amendments of the specification and claims are entered.

The rejection to the oath or declaration for non-initialed and/or dated alterations was maintained. A new oath is supplied herewith.

Applicants acknowledge that the following objections and rejections are withdrawn: the objection to the abstract of the disclosure for failing to describe the claimed invention; the objection to the improper use of trademarks in the specification; and the rejection of claims 88-96 under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,453,492.

Claim Rejections Maintained

The rejection of claims 88-96 under the judicially created doctrine of obviousness-type double patenting over claims 1-8 of U. S. Patent No. 6,803,453, was maintained. Applicants will file a terminal disclaimer upon indication of allowable subject matter in this application.

The rejection of claims 88-96 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, was maintained for reasons of record in the previous Office Action.

Applicants previously argued that determining whether antigen amino acid substitutions resulting from variations in the polynucleotide sequences of SEQ ID NOs:1, 5, 9, 11, 13 and 15 affect antibody binding would not require undue experimentation. Applicants argued that the specification describes the preparation of antigens as well as the production and testing of antibodies, and that one of skill can routinely identify or construct any antibody molecules meeting the limitations of the claims, and test them for binding to polypeptides encoded by polynucleotides that are at least 90% identical to SEQ ID NOs:1, 5, 9, 11, 13 and 15, or that hybridize to one of those polynucleotides. Applicants further argued that the Bowie et al., Geysen et al.,

and Colman references support the conclusion that many substitutions in the antigen encoded by polynucleotides having at least 90% identity to SEQ ID NOs:1, 5,9, 11, 13 and 15 are possible without affecting protein folding or antigen binding properties.

In response to applicants' arguments, the Examiner stated that:

> The claims read on fragments and variants of the polypeptides encoded by polynucleotide sequence of SEQ ID Nos:1, 5,9, 11, 13, and 15, including having deletion, substitution or insertion of one or plural amino acid residues in the sequence. Further, there is no limitation how long these molecules will be. The recitation "a complementary sequence thereto" encompasses a sequence of as few as three nucleotides. (Office Action, page 4, lines 14-19.)

Applicants respectfully disagree with the Examiner's statement that the claims read on fragments including as few as three nucleotides. A TGF-β binding protein would not be encoded by a three-nucleotide sequence. However, to ensure that the claims do not read on such embodiments, applicants have amended claim 88 to recite that the second polynucleotide comprises a nucleotide sequence that is fully complementary to SEQ ID NO:1, 5, 9, 11, 13 or 15. Applicants submit that this addresses the concern regarding fragments or length. The preamble to the claim clearly indicates that the first polynucleotide encodes a TGF-β binding protein and that the first polynucleotide hybridizes as indicated in the second part of the claim.

Regarding the Examiner's statement that one of skill "would evaluate all non-exemplified TGF-beta binding proteins for antibody binding activity," (page 5, lines 6-8) that is not a legal requirement. *In re Wands* (8 U.S.P.Q.2d 1400, Fed. Cir. 1988) does not suggest that one of skill would make every single possible antibody within the scope of the claims. Instead, the Court held that it would not require undue experimentation to "obtain antibodies needed to practice the claimed invention." (8 U.S.P.Q.2d at 1406.) *Wands* does not support or require the Examiner's interpretation that one would evaluate all non-exemplified TGF-β binding proteins. By analogy to *Wands*, enablement in the present case is met by the provision of the starting polynucleotide sequences (SEQ ID NO:1, 5, 9, 11, 13 or 15) and methods of hybridizing other sequences and expressing the TGF-β binding protein.

In summary, the Examiner seems to be proposing that one of skill would attempt to make every single possible embodiment. That is not the requirement of the enablement provision. *Wands* did not suggest that one would create every possible antibody, and applicants are not required to either.

Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 88-96 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, was maintained for reasons of record in the previous Office Action.

According to the Examiner, applicants describe an isolated antibody or antigen binding fragment thereof which binds to a TGF-β binding protein, encoded by a polynucleotide sequence selected from the group consisting of SEQ ID NOs:1, 5, 9, 11, 13, and 15, but not fragments and variants of TGF-β binding protein that the antibody binds to. The disclosure of SEQ ID NOs:1, 5, 9, 11, 13 is not sufficient to describe the common attributes or characteristics that identify all members of the genus, according to the Examiner. Applicants disagree.

Applicants cite to the recent Federal Circuit decision *Falkner v. Inglis*, Slip Op. 05-1324 (May 26, 2006) which clarified the written description law as it pertains to biological molecules. The court held that,

> (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

The court further stated that recitation of known structure is not required, citing *Capon v. Eshlar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005) and distinguishing *Eli Lilly* (*University of California v. Eli Lilly and Co.*, 119 F3d 1559, 43 U.S.P.Q.2d 1398 (1997)) on which the Examiner relied in the previous Office Action. The court also noted that "the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification." (*Falkner*, Slip. Op. at 17).

Applicants respectfully submit that the class of polynucleotides encoding TGF-ß binding protein is easily determinable from the art based on provision of SEQ ID NOs:1,

5, 9, 11, 13, and under *Falkner*, the application need not disclose the chemical structures. To list the complementary sequences would add "unnecessary bulk" to the application, a practice that *Falkner* rejects.

Applicants bring to the Examiner's attention U.S. Patent No. 6,562,949 issued on May 13, 2003, in which claim 1 reads as follows:

> 1. An antibody that specifically binds polypeptide with an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:2, wherein the percent identity is calculated using the GAP program with an unary comparison matrix, a 3.0 gap penalty, an additional 0.10 penalty for each symbol in each gap, and no penalty for end gaps, and said polypeptide binds a semaphorin selected from the group consisting of A39 semaphorin and AHV semaphorin .

Applicants submit that this claim language is comparable to the claim language under consideration in the present application. The percent identity in the claim quoted above relates to an amino acid sequence whereas the percent identity of applicants' claims is expressed in terms of the encoding polynucleotide. The 6,562,949 patent issued before the *Falkner* decision yet appears to be consistent with the holding of that decision.

Reconsideration and withdrawal of this rejection are respectfully requested.

If fees are believed necessary, the Commissioner is authorized to charge any required fee, deficiency or credit any overpayment to Deposit Account No. 04-0258. A duplicate copy of this document is enclosed.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
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